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The causes of autism spectrum disorders

Multiple factors have been identified, but a unifying cascade of events is still elusive

Autism is a developmental disability with onset in infancy. Its clinical presentation is characterised by impairments in reciprocal social interaction and in communication with others, and by a preference for repetitive, stereotyped behaviours. Our understanding of the clinical picture of autism has changed dramatically over the past decade thanks to a much greater appreciation of the possible range of behaviours seen at different ages and degrees of functioning. Another key change has been the appreciation that several closely related "disorders" exist that share these same essential features but differ on specific symptoms, age of onset, or natural history. These disorders, which include Asperger syndrome, atypical autism, and disintegrative disorder are often conceptualised as lying on a spectrum with autism (hence the popularity of the term "autism spectrum disorders"). Current estimates of the prevalence of autism are 16 per 10 000, but this estimated prevalence increases to 63 per 10 000 when all forms of autism spectrum disorders are included[1]—much higher than previously reported.

Along with these changes in taxonomy has been a greater understanding of the causes of autism, although, admittedly, the picture of the cascade of structural and biochemical events that culminate in the disorder is still not clear. Surely, however, we are much further ahead today than we were some years ago when blame was squarely placed on the shoulders of mothers who, it was claimed, were cold and indifferent to their infants. The distress caused by these claims is a painful reminder of the need for evidence based information on causation for all parents who have children with developmental or psychiatric disorders.

Developmental delay, epilepsy, dysmorphic features, obstetric complications, an unequal sex ratio, and extremes of head size[1 2 w1] represent non-specific signs that autism is a neuropsychiatric disorder. Perhaps the most important advance in changing our understanding of the cause of autism was the discovery that genetic factors have a key role. In 1977, Folstein and Rutter published the first twin study in autism and showed that the concordance rate in identical twins was very much higher than in non-identical twins.[3] This finding has now been replicated several times and is well established.[4] But the genetics of the disorder must be complex, as the mode of transmission does not follow any recognisable pattern. Modelling studies have shown that multiple genes in interaction probably account for the genetic complexity underlying the disorder.[w2 5]

These data do not exclude an environmental risk factor as well; as long as it is understood that "environmental" in this context can include any event after fertilisation. The only environmental factors for which we have preliminary evidence of such causation are thalidomide induced embryopathy[w3] and anticonvulsants taken during pregnancy.[w4] In spite of recent publicity, there is good epidemiological evidence that the measles, mumps, and rubella vaccine is not an environmental risk factor for autism.[6]

The strong genetic effects observed in family and twin studies have encouraged investigators to conduct linkage and association studies that attempt to identify actual susceptibility genes. Although several promising findings are based on candidate gene studies (particularly in the region 15q11-13[w5 w6]), these have yet to be replicated consistently. Several genome-wide linkage studies have found that regions on chromosomes 2, 7, and 13 may contain one or more susceptibility genes but actual susceptibility genes have not yet been identified.[7 w7] Further progress may depend on collecting very large sample sizes. Another helpful approach is to identify more immediate biological effects of these putative susceptibility genes. Postmortem examinations and studies using magnetic resonance imaging have found larger volumes of white matter in general and subtle structural changes in cell density and alignment, particularly in the limbic system.[w8 8] Functional imaging studies have also reported atypical activation of the amygdala and surrounding structures in response to social stimuli.[w9 9]

A minority of children with autism have a comorbid disorder of the central nervous system that presumably "causes" the disorder. In total, these comorbid conditions probably account for only 10-15% of cases,[10] but they should be kept in mind as their diagnosis will have clinical implications.[11 w10] In terms of comorbid medical disorders, good evidence now exists that disturbances of the gastrointestinal system are not more common in children with autism than in the general population of children.[w11] No causative factors have been found to differentiate children with autism from children with other disorders on the spectrum such as Asperger syndrome. Good evidence exists that these related conditions arise from a common familial, presumably, genetic mechanism.[12]

It is gratifying to see that research into the causes of autism has helped to temper the guilt so often experienced by parents when the disorder was considered to be psychogenic in origin. However, the difficulty of conducting sound studies of causation has now led

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some healthcare practitioners to encourage parents to act on very poor quality data and vigorously pursue hypothetical causes. It is generally anticipated, however, that with newer technologies and study designs, the risk factors initiating the causal chain that culminates in this profoundly disabling disorder will soon be identified. The great hope is that from this understanding, more definitive treatments can be developed to improve long term outcomes for all children with autism spectrum disorders.

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Governance for NHS foundation trusts

Mr Milburn's flawed model is a cacophony of accountabilities

Now that England's health secretary, Alan Milburn, has published his *Guide to NHS Foundation Trusts*,[1] it is apparent that the proposed model is more radical in its implications but also more problematic in its implementation than had been anticipated. It is radical in that it is based on a new notion of social ownership modelled on cooperative societies and mutual organisations: the rhetoric of devolving power in the NHS is, in effect, to be institutionalised by transferring control to the "local communities" served by foundation trusts. Moreover, the first generation of foundation trusts is seen as preparing the way for their status becoming the norm in the NHS in time. If so, then the relation between centre and periphery in the NHS could change dramatically. It is problematic, however, in that the proposed system of governance for foundation trusts could make those working in them look back nostalgically to the days when their chief concern was about the heavy hand of central government.

Some of the initial fears about foundation trusts were clearly misplaced. They do not represent a backdoor form of privatisation. They will not be given a free hand to expend their facilities for treating fee paying patients: the percentage of income derived from this source is to be capped. They will be obliged to offer a set of "regulated services" to ensure that NHS commissioners, and eventually individual consumers, have an adequate menu of choice. And, of course, they will have to comply with national clinical and quality standards. Worries that the autonomy of foundation hospitals will be severely circumscribed by tight regulation[2] have more substance than apocalyptic charges that the new model threatens the principles of the NHS or will lead to a two tier service. As it is, the NHS is a multiple tier service, with trusts varying considerably in the quality of the services provided: witness the notorious star system.

It is the proposed model of governance that prompts serious doubts. Ideologically it seems adaptable: it harks back to a strong tradition in socialist writing yet also has the sympathetic attention of the London based Institute of Directors, the leading membership organisation for directors who are responsible for the strategic direction of companies.[3] But translated into a plan of action it is seriously flawed. Consider, first, the internal governance of trusts. They will have boards of governors, of which most will be elected by "the patient and public membership," some from the "employee membership," and the rest will be nominated by "partner organisations" such as local primary care trusts or universities. In turn, the board of governors will choose the chief executive and the non-executive members of the management board responsible for the day to day running of the trust.

But who will be the members electing the board of governors? Seemingly, they will be self selected. Anyone who is living in the local area, who has been a patient of the trust, or who is an employee will be eligible to register and vote. Details on how to organise all this is left to aspiring foundation trusts. The first safe prediction therefore is that the membership will be unrepresentative. It will be skewed towards members with intense but possibly atypical views about the NHS and will reflect the organising activities of pressure groups. The second safe prediction is that apathy will rule. This is what the history of the cooperative movement documents[4] and what the recent experience of mutual organisations such as building societies illustrates: in the latter case, members took an active interest only when the issue of demutualisation came up.

Also, the model conflates two quite different types of mutual organisations—cooperatives of producers and cooperatives of consumers. Combining the two internalises the inevitable tensions between the two sets of interests. It might have been wiser to have

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